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10/533,584	05/03/2005	Hideki Yoshikawa	2005_0714A	5037

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EXAMINER	
NATARAJAN, MEERA	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,584	YOSHIKAWA ET AL.	
	Examiner	Art Unit	
	Meera Natarajan Ph.D.	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05/03/2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/03/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on 03/20/2007 is acknowledged.

2. Applicant amended claims 1-7 from an agent to a "method of treating". The amendments are acknowledged, however by changing the claims to process claims Applicant has constructively elected the subject matter of Group II. Therefore all claims will be examined. Any claims directed to the product of Group I presented in later prosecution will be withdrawn from consideration as directed to a non-elected invention.

3. Claims 1-9 are examined on the merits.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 7 recites "wherein the humanized antibody is a humanized #23-57-137-1 antibody". It is unclear whether #23-57-137-1 antibody is already a humanized antibody or whether the antibody being claimed is a humanized antibody of #23-57-137-1? Clarification is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

a) Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirements for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

The genus being claimed in the current application is "substance" which inhibits binding of parathyroid hormone related peptide to a receptor thereof. The application does not provide any exemplary species of the genus, and provides no identifying characteristics other than a functional limitation (inhibits binding). Applicant only discloses the possession of an "anti-PTHrP" antibody, but not all "substances" which inhibit binding. Based on the lack of any species, and the lack of the identification of any characteristics other than the functional limitation, the application provides insufficient descriptive support to demonstrate possession of the claimed genus.

6. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing apoptosis *in vitro* by inhibiting binding of parathyroid hormone related peptide to a receptor thereof, does not reasonably provide enablement for *in vivo* methods involving administering to a subject a substance which induces apoptosis by inhibiting binding of parathyroid hormone related peptide to a receptor thereof to treat chondroma and chondrosarcoma. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant is claiming a method of using a substance which inhibits binding of parathyroid hormone related peptide to a receptor thereof, wherein the method practiced *in vivo* is used to treat chondroma and chondrosarcoma.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230

U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. The factors considered most relevant in this case are the breadth of the claims, the state of predictability of the art, and the working examples and guidance presented in the application.

a) In the current application the Wands factor of "predictability or unpredictability of the art" does not support a finding of enablement. All evidence stated in the application is *in vitro* data. The application nowhere provides any working examples of *in vivo* results supporting the claimed invention that administering to a subject an antibody which inhibits binding of parathyroid hormone related peptide to a receptor will treat chondroma and chondrosarcoma. It also well known in the art that cancer treatment is an unpredictable art in itself. Zips et al. [In Vivo. 2005 Jan-Feb;19(1):1-7.] discloses; "It is obvious that cells in culture represent an artificial and simplified system. Unlike the situation *in vitro*, a tumor is a 3-dimensional complex consisting of interacting malignant and non-malignant cells. Vascularization, perfusion and, thereby drug access to the tumor ceils are not evenly distributed and this fact 'consists' an important source of heterogeneity in tumor response to drugs that does not exist *in vitro*. Therefore, prediction of drug effects in cancer patients based solely on *in*

vitro data is not reliable and further evaluation in animal tumor systems is essential." Therefore, the skilled artisan seeking to administer anti-PTHrP as a treatment method for chondroma and chondrosarcoma would have to engage in undue experimentation to determine how to practice/use the claimed invention.

b) Applicant also lacks guidance on how the claimed invention may be administered to patients suffering from chondroma and chondrosarcoma. What constitutes an effective dose of the antibody, what would be sufficient to provide a therapeutic effect, and what host responses may be elicited by the administration of the antibody. Essentially, the skilled artisan, given applicant's disclosure, would need to practice undue trial and error experimentation in order to develop the method such that it could be used to treat chondroma or chondrosarcoma.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 8 and 9 are rejected under 35 U.S.C. 102(a) as being anticipated by Miyaji et al. ("Apoptosis inducing effect and differentiation accelerating effect on chondrosarcoma cell line of monoclonal antibody to parathyroid hormone-related protein"; The Japanese Cancer Association Sokai Kiji, August 25, 2002, p 174 of record in the May 5, 2005 IDS). Applicant is claiming a method of inducing apoptosis in

chondroma and chondrosarcoma cells by administering anti-parathyroid hormone related peptide antibody. Miyaji et al. teaches the use of a monoclonal antibody to parathyroid hormone-related peptide that induces apoptosis in a chondrosarcoma (see the translation submitted with the IDS). Therefore, the reference teaches each and every limitation of claims 8 and 9.

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meera Natarajan Ph.D. whose telephone number is 571-270-3058. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

MARY MOSHER
SUPERVISORY PATENT EXAMINER

4-30-07